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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,375	02/28/2002	Cecil W. Forsberg	6580-270	9974

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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 02/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,375	FORSBERG ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *36-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☒ Claim(s) *13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 08/30/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Sequence Compliance Notice

DETAILED ACTION

Applicant's election without traverse of Group 1, claims 1-35 in the reply filed on 12/23/2004 is acknowledged.

Claims 36-57 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/23/2004. Claims 1-57 are pending and claims 1-35 are under consideration in the instant office action.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Embedded hyperlinks are found throughout the specification. For example see page 21, lines 22 and 26.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The nucleic acid and polypeptide sequences throughout the specification require Sequence Identifier Numbers. For example, see page 20, line 13 and Table 12. Each of the individual sequences in Table 12 requires a sequence identifier.

Applicants must file a "Sequence Listing" accompanied by directions to enter the listing into the specification as an amendment. Applicant also must provide statements regarding sameness and new matter with regards to the CRF and the "Sequence Listing."

Applicant is requested to return a copy of the attached Notice to Comply with the reply. Failure to fully comply with the sequence rules in response to the instant office action will be considered non-responsive.

Claim Objections

Claim 13 objected to because of the following informalities: The word "transgene" in line 2 is misspelled.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic non-human mammal whose genome comprises a transgene comprising a gene encoding a phytase operably linked to a mammalian salivary gland specific promoter wherein the animal is a pig, goat, sheep, cow, or horse, wherein the phytase is expressed in the salivary gland of the animal does not reasonably provide enablement for any other animal encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The breadth of the claims is so broad as to encompass numerous transgenic mammal species as well as fish and poultry species wherein the animal comprises a transgene encoding any protein operably linked to any salivary gland specific promoter that is derived from any species of animal (claims 1 and 13). Claim 13, however, fails to require the presence of any promoter at all and therefore encompasses a promoterless transgene. Some claims limit these genera. Claims 3,15 and 16 limit the salivary gland specific regulatory sequences to a PSP (also claim 4), a PRP (also claim 5) or a salivary amylase promoter. However, these claims are so broad as to encompass such promoters from any species of animal, including non-

mammalian species. Claims 5 and 7 limit the PSP and PRP promoters to those derived from mouse and rat, respectively. Claim 9 limits the animal species to pig. Claim 10 limits the protein encoded by the transgene to a phytase. Claim 11 limits non-enabled genera of claim 1, with the exception that claim 11 continues to broadly encompass PSP and PRP promoters from non-mammalian species. Claims 12 and 18 limit the transgene to those set forth by SEQ ID NO:s 3,5 and 7. Claims 19-35 are method claims having the similar breadth as the product claims. The methods are drawn to expressing a protein by introducing a transgene into an animal. Claims 17,19-22 and 24-29 require expression of the transgene wherein expression is anywhere in the gastrointestinal tract. Claims 1,8-16 and 18 fail to require transgene expression

The specification has taught four different transgenic animals. The first 3 are mice comprising 3 different salivary specific transgenes. The first and second mouse comprise a transgene comprising the APPA (phytase) gene operably linked to the inducible R15-PRP promoter that is derived from rat. The first and second mouse differ in that the transgene of the second mouse also comprises an intronic sequence that appears to lower transgene expression levels (see pages 16-18). The third mouse is one whose genome comprises a transgene comprising the APPA (phytase) gene operably linked to the constitutively active Lama2 promoter that is derived from the mouse PSP gene (see pages 22-23). The fourth animal is a transgenic pig comprising the same transgene as the third mouse, that is the APPA (phytase) gene operably linked to the constitutively active Lama2 promoter that is derived from the mouse PSP gene (see pages 23-27).

The specification has failed to provide the guidance necessary to carry out the claimed invention with respect to the broad genera encompassed by the claims. The specification has not taught generating any transgenic fish or poultry species. The specification has not taught transgenic expression of any gene other than the phytase gene. Furthermore, the specification has not taught that salivary-specific promoters from non-mammalian species have conserved structure and/or function and therefore has not taught that non-mammalian salivary-specific promoters will promote salivary-specific expression in mammals or that mammalian salivary-specific promoters will promote salivary-specific gene expression in non-mammalian species such as fish and poultry species.

The art at the time of filing and the specification clearly indicate a large variation in the amount of expression from the transgenes in various species of animals and within species of animals. For many transgenes, the position of integration has a large effect on the level of expression of a particular transgene, as indicated by the large variation of expression in the instant invention (see Table I, for example). Some transgenes also have different effects in different species of animals. For example, several animal models of human disease have relied on transgenic rats when the development of mouse models was not feasible. Mullins (1990, Nature, Vol. 344, 541-544) produced outbred Sprague-Dawley x WKY rats with hypertension caused by expression of a mouse *Ren-2* renin transgene. Hammer (1990, Cell, Vol. 63, 1099-1112) describes spontaneous inflammatory disease in inbred Fischer and Lewis rats expressing human class I major histocompatibility allele HLA-B27 and human β_2-microglobulin transgenes. Both investigations were preceded by the failure to develop human disease-like symptoms in transgenic mice expressing the same transgenes that successfully caused the

desired symptoms in transgenic rats. Thus, the combination of elements (protein, promoter, species of protein, and species of transgenic animal) required to obtain a desired effect were not predictable at the time of filing.

The art at the time of filing with respect to transgenesis in poultry species, such as chick, held that the techniques were highly underdeveloped. Foremost, mammalian transgenic techniques are not easily applied to poultry species because the bird develops externally in a shelled egg (see Sang, 2004, Mech. Dev., Vol 121, pages 1179-1186, specifically, page 1179, col. 1). There are limitations with respect to transgene delivery and transgene size in using host shells and albumin as culture medium (see paragraph bridging pages 1179-1180). Use of an ES cell approach as is done with mice is complicated by the fact that PGCs are thought to be determined before the egg is laid and fail to contribute to the germ line after being in culture for more than one week. However, methods have been developed that allow for development of germ line chimeras using blastodermal cells (paragraph bridging pages 1180-1181 and paragraph bridging col.1-2 of page 1181). Despite these developments, genetically modification of cells from cell culture has failed to allow for germline transmission. Use of PGCs to generate germ line chimeras has also been successful, however, transgenic birds have not been made with such a technique (page 1182, col. 1, paragraph 2). Low levels of transgene transmission through the germ line using avian viral vectors has been demonstrated (see page 1182, col. 2). Currently, research is focusing on identifying more efficient vectors that will make the technique more feasible. (See also Mozdziak, 2994, Dev. Dynam., Vol. 229, pages 414-421 for additional review).

The art at the time of filing with respect to transgenic fish was that promoters of heterologous origin were not efficiently or effectively expressed (refer to Udvadia, 2003, Dev. Biol. Vol. 256, page 7, col.1, paragraph. 4). In fact, it is thought that non-zebrafish promoters are often silenced when introduced into the genome of zebrafish (see Higashijima, 1997, Dev. Biol., Vol. 192, pages 289-299). Higashijima found that use of zebrafish derived promoters in zebrafish resulted in much more consistent expression with higher fidelity across a large number of independently derived lines (refer to paragraph bridging col. 1-2 of page 297). Therefore, it was recognized in the art that use of heterologous promoters in fish was highly unpredictable as to whether the transgene would be expressed, silenced, or expressed to a particular level and in a specific desired pattern.

Finally, the art at the time of filing with respect to salivary-specific promoters failed to support the presence and evolutionary conservation of salivary-specific promoters among diverse species such as mammals, birds and fish. For example, the salivary amylase promoter has been highly characterized with respect to evolutionary conservation and in addition to a large to degree of evolutionary change in the promoter in primate mammals, it appears that either non-primate mammalian salivary amylase was acquired independent of that of primates or the gene became extinct in several mammalian lineages (Samuelson, 1996, Mol. Biol. Evol., Vol. 13, pages 767-779, specifically page 778, col. 1, paragraph 2). According to Samuelson, all vertebrates express amylase in the pancreas but not all species of primates, rodents, lagomorphs and chiropterans do. Samuelson does note that despite recent evolutionary change to the human salivary amylase promoter, this promoter is functional and salivary-specific in transgene mice. With respect to the PSP and PRP promoters encompassed by the

claims, the art at the time of filing demonstrated that the expression pattern of rat and mouse PSP are conserved (Saito, 1999, Jour. Immunol., Vol. 162, pages 2488-2494), however, there is no evidence of record indicating the existence or the conservation of PRP or PSP genes or promoters in non-mammalian species.

1) The specification is not enabling for the claimed poultry and fish species of animal or for use of a non-mammalian salivary-specific promoter in mammalian species. The specification has demonstrated that 2 different promoters, the rat R15 PRP and mouse PSP promoters, are expressed in transgenic mice and pig. While this is considered evidence of conservation of promoter activity among mammalian species, these teachings fail to overcome the underdeveloped state of the art with respect to avian transgenesis and the state of unpredictability of transgene expression using heterologous promoters in fish. Therefore, the specification is not enabling for the full breadth of the claims.

The specification does not teach how to make the claimed fish and birds comprisinf the broad genera of salivary-specific promoters. As set forth above, the state of the art was highly underdeveloped with respect to avian transgenesis and the use of heterologous promoters in fish was highly unpredictable. It would require undue experimentation for one of ordinary skill in the art at the time of filing to determine how to make a transgenic fish or transgenic poultry species such that phytase is appropriately expressed in the salivary gland. Furthermore, without demonstration of conservation of salivary-specific promoter activity between mammals and poultry species and fish, it cannot be determined that non-mammalian salivary-specific promoters, would be expressed appropriately in mammalian species as broadly encompassed by the claims. The evidence of record fails to set forth any avian or fish salivary promoters or

that they would be functional in heterologous species, including mammals. Therefore, it would require undue experimentation to determine how to use a non-mammalian salivary-specific promoter to express phytase in the salivary gland of any transgenic species.

2) The specification is not enabling for using the transgenic non-human animals encompassed by the claims wherein expression of the transgene does not occur (claims 1,8-16 and 18) or occurs anywhere other than in the salivary glands (claims 17,19-22,24-29). The claims fail to recite that the animals express the transgene or to require that expression occur in the salivary glands. The specification has taught the production of transgenic animals using salivary specification promoters and use of the animals in producing phytase in the salivary glands to aid in digestion of phytase in food products. The specification has not taught how to use animals that do not express the transgene or animals that express the transgene in a tissue other than the salivary gland. It is specifically noted that claims 17,19-22 and 24-29 require expression in the gastrointestinal tract or pancreatic gland and do not require salivary gland expression. The specification and art at the time of filing teach a number of salivary-specific promoters and fails to support expression in other gastrointestinal tissues. The art also has established that the salivary amylase and pancreatic amylase genes are distinct and separate (Samuelson, 1996, page 767, col. 1, paragraph 1). Therefore, the evidence of record does not support expression in any other part of the gastrointestinal tract of the animal using a salivary gland specific regulatory sequence as claimed. It would require undue experimentation for one of ordinary skill in the art at the time of filing to determine what salivary-specific promoter constructs would effectively express a transgene in the gastrointestinal tract or pancreatic gland

of a transgenic animal. It would also require undue experimentation for one of ordinary skill in the art to use an animal that does not express the claimed transgene.

3) The specification is not enabling for a transgene encoding any protein (claims 1-9,11,19-24,29-31,35) or any glycoprotein (claims 25 and 32). The specification teaches making a transgenic mouse or pig expressing a phytase in the salivary gland. These animals are to be used to hydrolyze dietary phytate that normally is not digested and is excreted by the animal. Excretion of phytate has harmful implications on the environment. The specification does not teach the skilled artisan to use the claimed animals wherein any protein is encoded by the transgene other than a phytase. As set forth by the art at the time of filing, the expression and resulting phenotype of a transgene in an animal is highly unpredictable. Therefore, one of ordinary skill in the art would not know what a transgenic animal expressing a transgene encoding any protein would look like or what use it would have. It would require one of ordinary skill in the art at the time the invention was made to determine how to use the claimed animals comprising a transgene encoding any protein other than a phytase.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1) Claims 1-5,8,9,19-25,29-32 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mikkelsen, 1992, Nucl Acids Res., Vol. 20, pages 2249-2255; IDS) in view of Velander (1992, PNAS, Vol. 89, pages 12003-12007).

Claims are drawn a transgenic animal and methods of making said animal, wherein the animal is a pig, goat, sheep, cow, horse, fish or poultry, that carries in the genome of its somatic and germ cells a transgene encoding any protein operably linked to a regulatory sequence for salivary gland specific expression.

Mikkelsen taught making transgenic mice comprising a transgene encoding human factor VIII operably linked to a salivary-specific Lama PSP regulatory region (page 2250, col. 2, last paragraph-page 2251, col. 2, paragraph 1). Mikkelsen taught introducing a transgene into a mouse embryo and transferring the embryo into a foster or pseudopregnant female mouse and developing the embryo into a transgenic mouse (page 2250, col. 1, paragraph 5). The mice secrete Factor VIII into the saliva (see page 2251, col. 2 paragraph 2-page 2252, col. 2, paragraph 2). Mikkelsen taught that there were multiple regulatory regions within the Lama DNA, satisfying the requirements for a first and second regulatory sequences of claim 8. Factor VIII is a glycoprotein as required by claims 25 and 32. Mikkelsen did not teach making a transgenic pig, goat, sheep, cow, horse, fish or poultry using the factor VIII-lama construct. Mikkelsen did not teach extracting the protein.

However, Velander taught making transgenic pigs expressing human protein C in the mammary gland that was secreted into the milk and later purified.

One of ordinary skill in the art at the time the application was filed would have been motivated to combine the teachings of Mikkelsen regarding transgenic expression of a desired

protein in the salivary gland of mice with the teachings of Velander to generate a transgenic pig expressing a desired protein in saliva. One of ordinary skill in the art would have been motivated to make such a combination as Mikkelsen taught that salivary expression of proteins is useful as a bioreactor to isolate quantities of a protein and that salivary expression has an advantage over use of mammary specific expression that is often used as a bioreactor because both sexes of animal can be used (page 2249, col. 2, paragraph 2). Mikkelsen taught similarities between mammary and salivary expression and secretion of proteins (page 2249, col. 2, paragraph 2). Furthermore, pigs are larger than mice and would be a greater source of protein.

One of skill in the art would have had a reasonable expectation of success in combining the teachings of Mikkelsen with those of Velander because strong salivary-specific promoter elements were known as were the techniques of making transgenic pigs.

Thus, the claimed invention is clearly *prima facie* obvious in the absence of evidence to the contrary.

2) Claims 1,10,11,13-17,19,26,27,30 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mikkelsen, (1992, Nucl Acids Res., Vol. 20, pages 2249-2255;IDS) in view of Velander (1992, PNAS, Vol. 89, pages 12003-12007), and further in view of Pen (1993, Bio/technology, Vol. 11, pages 811-814; IDS) as evidenced by Laursen (1997, Gene, Vol. 198, pages 367-372;IDS).

Claims are drawn a transgenic animal and methods of making said animal, wherein the animal is a pig, goat, sheep, cow, horse, fish or poultry, that carries in the genome of its somatic and germ cells a transgene encoding any protein operably linked to a regulatory

sequence for salivary gland specific expression. Claims 10,11,13,15-17,26 and 34 comprise the additional limitation that the protein encodes a phytase. Claims 14 and 27 limit the phytase to the *E. coli* AppA phytase.

Mikkelsen taught making transgenic mice comprising a transgene encoding human factor VIII operably linked to a salivary-specific Lama PSP regulatory region (page 2250, col. 2, last paragraph-page 2251, col. 2, paragraph 1). Mikkelsen taught introducing a transgene into a mouse embryo and transferring the embryo into a foster or pseudopregnant female mouse and developing the embryo into a transgenic mouse (page 2250, col. 1, paragraph 5). The mice secrete Factor VIII into the saliva (see page 2251, col. 2 paragraph 2-page 2252, col. 2, paragraph 2). Mikkelsen taught that there were multiple regulatory regions within the Lama DNA, satisfying the requirements for a first and second regulatory sequences of claim 8. Factor VIII is a glycoprotein as required by claims 25 and 32. Mikkelsen did not teach making a transgenic pig, goat, sheep, cow, horse, fish or poultry. Mikkelsen did not teach using the rat PRP promoter. Mikkelsen did not teach using a transgene encoding phytase. Mikkelsen did not teach extracting the protein.

However, Velander taught making transgenic pigs expressing human protein C in the mammary gland that was secreted into the milk and later purified using a transgene encoding human protein C operably linked to a mammary specific promoter. Velander did not teach using a transgene encoding a phytase.

However, Pen taught transgenic seeds expressing phytase. Pen taught that seeds expressing a transgene encoding phytase was essentially a bioreactor in that they provide the animals that eat the seed with phytase, which optimizes phosphorus utilization and reduces

excretion of phosphate in pigs (see page 811, col. 1, paragraph 2). Pen did not specifically teach using the E. coli AppA phytase, however, there is no evidence of record to indicate that this phytase is not equivalent to any other phytase and is merely a choice of design.

One of ordinary skill in the art at the time the application was filed would have been motivated to combine the teachings of Mikkelsen regarding transgenic expression of a desired protein in the salivary gland of mice with the teachings of Velander to generate a transgenic pig expressing a desired protein in saliva and with the teachings of Pen wherein the desired protein is a phytase. One of ordinary skill in the art would have been motivated to make such a combination as Laursen taught that expression of enzymes in the gastrointestinal tract, including the salivary glands, of farm animals as a way of improving food utilization. Accordingly, as set froth above, Pen taught that phytase aids in the digestion of phytates, providing animals with phosphorus and that the abundant presence of phosphate in the environment as a result of undigested phytate has an unfavorable impact on the environment.

One of skill in the art would have had a reasonable expectation of success in combining the teachings of Mikkelsen with those of Velander because strong salivary-specific promoter elements were known as were the techniques of making transgenic pigs. One would expect that use of the phytase gene would provide the additional benefits set forth by Pen as prior methods of adding phytase to feed were successful and secretion from salivary glands adds the phytase to food prior to digestion.

Thus, the claimed invention is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632

AU1632

Application No.: 09/926375

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [ ] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

- [X] 7. Other: The polypeptide and nucelic acid sequences throughout the specification require sequence identifier numbers.

If Necessary, Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

Gail Winston AU1637

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE